

REMARKS

The present remarks are responsive to the Examiner's Office Action dated September 13, 2006 and to the interview conducted between Examiner Isabella and Applicants' representative on November 20, 2006. Claims 1, 4-7, 9, 11-12, 14, 16-21 and 42-54 are pending in the present application, with Claims 2-3, 8, 13, and 22 being canceled herein, Claims 1, 4-7, 14, 16-18, and 21 being amended and new Claims 42-54 added. Reconsideration of the application in view of the foregoing amendment and following comments is respectfully requested.

Amended Specification

Applicants have amended paragraph [0014] as follows:

1. In the sentence that begins "Dealloying a layer of an implantable device provides a porous layer..." the sentence has been amended to read "Dealloying a layer of an implantable device provides a nanoporous sponge layer..." No new matter has been added. Support for this amendment of the specification can be found in Figures 2A and 2B, which depict sponge layers. The scale provided in each of Figures 2A and 2B support the amendment of "porous" to "nanoporous".
2. Prior to the last sentence of the paragraph, Applicants have inserted the sentence "In some instances, the nanoporous sponge layer may be characterized morphologically as coalesced clusters or islands interconnected by ligament structures." No new matter had been added by this amendment, as support for this amendment is also depicted in Figures 2A and 2B. These descriptive terms for the porous sponge layer are consistent with descriptions found in the Erlebacher article on pg. 451, second column, second full paragraph, which states "Central to this description is the the [sic] coalescence of gold adatoms into stable clusters. The spacing between the 'islands' in the initial states of dissolution is close to the spacing between ligaments in the final porous structure."¹ The full citation to the Erlebacher article is provided in paragraph [0014]. Thus, the foregoing

¹ Erlebacher refers to gold atoms lacking adjacent lateral atoms as "adatoms." Please see Erlebacher pg. 451, second column, first full paragraph.

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characterization of the structure was known at the time of applicant's invention to be an inherent result of applicant's disclosed dealloying process.

Amended and New Claims

Applicants have amended Claims 1, 4-7, 14, 16-18, and 21 to clarify the claimed subject matter. Applicants have also added new dependent Claims 42-53. Support for the claim amendments and new claims are identified below:

Claim No.	Amended/New Subject Matter	Support
1	<i>sacrificial component</i>	¶[0021]
	<i>structural component</i>	¶[0021]
	<i>selectively removing</i>	¶[0022]
	<i>matrix with tortuous pathways</i>	Figs. 2A and 2B
4	<i>deleted device</i>	¶[0005]
5	<i>tubular</i>	¶[0005]
6	<i>deposited</i>	¶[0006]
7	<i>deposited onto</i>	¶[0006]
14	<i>selectively removing</i>	¶[0022]
	<i>sacrificial component</i>	¶[0021]
	<i>removing</i>	¶[0021]
16	<i>tortuous pathways of the matrix</i>	Figs. 2A and 2B
17	<i>therapeutic agent</i>	¶[0022]
18	<i>deleted at least one</i>	¶[0022]
21	<i>inner surface</i>	¶[0020]
	<i>tubular stent</i>	¶[0005]
42	<i>nanoporous</i>	Figs. 2A and 2B
43	<i>dealloying</i>	¶[0014]
44	<i>cobalt-chromium</i>	¶[0017]
45	<i>L605</i>	¶[0017]
46	<i>silver-gold alloy</i>	¶[0018]

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Claim No.	Amended/New Subject Matter	Support
47	<i>stainless steel alloy</i>	¶[0021]
48	<i>316L stainless steel</i>	¶[0021]
49	<i>nickel-titanium</i>	¶[0021]
50	<i>second alloy and second porous layer</i>	¶[0016]
51	<i>second alloy deposited on porous layer</i>	¶[0016]
52	<i>different atomic composition</i>	¶[0016]
53	<i>different porosity</i>	¶[0016]
54	<i>alloy deposited on inner and outer surfaces</i>	¶[0016]

Response to the Rejections under 35 U.S.C. §102(b)

The Examiner rejected Claims 1 and 2 under 35 U.S.C. § 102(b) as being anticipated by U.S. Patent No. 3,190,749 to Fleming. According to the Examiner, Fleming discloses a method of fabricating a metal substrate including providing at least one alloy and removing at least one component of the alloy to form at least one porous layer. However, Fleming does not disclose the use of such processes on an implantable medical device, as required by Claim 1. Indeed, the only disclosed functions for the porous structures in Fleming is as “catalysts or as lubricant accomodators” (Fleming, Col. 1, lines 16-21). No medical-related application is disclosed anywhere in the patent. Because Fleming fails to disclose each and every claim limitation of Claim 1, Claim 1 is not anticipated by Fleming.

Claim 2 is patentable for at least the same reasons that Claim 1 is patentable, and is also patentable for the unique combination of features that Claim 2 recites.

In view of the foregoing, Applicants respectfully submit that Claims 1 and 2 comply with the requirements of 35 U.S.C. §102(b).

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Response to the Rejections under 35 U.S.C. 103(a)

1. Claims 1-9, 11-4, 16-18, 21 and 22

The Examiner rejected Claims 1-9, 11-14, 16-18, 21 and 22 under 35 U.S.C. §103(a) as obvious over Gertner et al. (U.S. Pat. Pub. No US2005/0106212) in view of Fleming or Sieradzki (U.S. Pat. No. 4,977,038).

According to the Examiner, Gertner et al. discloses a method for forming a stent, including micro-pitting the surface of the stent for receipt of bioactive agents. Although Gertner discloses a pitting process for preparing a substrate to promote adhesion (*See Gertner ¶[0092]*), this pitting process relates only to the preparation of the substrate for adhesion of the actual porous layer disclosed by Gertner. The porous layer disclosed in Gertner, i.e. the “metal matrix” for retaining the bioactive material (see Gertner abstract), is formed by using an electrochemical solution comprising metal ions and bioactive material in a deposition bath (*See Gertner ¶[0091]*). Thus, Gertner’s process for forming a porous layer is a co-deposition process, not a removal process as required by Claim 1.

According to the Examiner, Sieradzki et al., like Fleming, teaches forming porous metallic substrate by removing certain alloyed portions creating a porous matrix. The Examiner states that it would have been obvious from the teachings of Fleming or Sieradzki et al. to provide a non-corrosive surface which would reduce unwanted leachings of metallic ions in vivo.

Although the Examiner asserts that a motivation exists for combining Fleming or Sieradzki with Gertner, the Applicants respectfully disagree. “Before the PTO may combine the disclosures of two or more prior art references in order to establish *prima facie* obviousness, there must be some suggestion for doing so, found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art.” *In re Jones*, 958 F.2d 347, 351 (Fed. Cir. 1992) (*citing In re Fine*, 837 F.2d 1071, 1074 (Fed. Cir. 1988)). “Even if all its limitations could be found in the total set of elements contained in the prior art references, a claimed invention would not be obvious without a demonstration of the existence of a motivation to combine those references at the time of the invention. *See Ecolochem, Inc. v. S. Cal. Edison Co.*, 227 F.3d 1361, 1371 (Fed.Cir.2000). This requirement prevents a court from labeling as obvious in hindsight a solution that was not obvious to one of ordinary skill at the time of the invention.” *National Steel Car, Ltd. V. Canadian Pacific Railway, Ltd.*, 357 F.3d 1319, 1337

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(Fed. Cir. 2004). Here, the removal processes of Fleming and Sieradzki to form a porous layer are directly opposite/contradictory/incompatible with the deposition process of Gertner. Thus, on its face, the combination of Fleming's or Sieradzki's removal process with the Gertner's deposition bath or metallic matrix appears non-functional and therefore inoperative. It is well established that a combination of references that would produce a seemingly inoperative device "cannot serve as predicates for a prima facie case of obviousness." *McGinley v. Franklin Sports, Inc.*, 262 F.3d 1339, 1354 (Fed. Cir. 2001) (citing *In re Sponnoble*, 405 F.2d 578, 587 (C.C.P.A. 1969) (references teach away from combination if combination produces seemingly inoperative device)). For this reason, the Applicants disagree that the Examiner has established a prima facie case of obviousness, due to the contradictory processes for forming a porous layer disclosed in the Gertner with Fleming or Sieradzki.

Furthermore, the Applicant's position is supported by the specification of Gertner, which teaches away from pore-forming processes that pre-form a porous surface rather than simultaneously co-depositing metallic matrix and bioactive agent. A reference is said to teach away "when a person of ordinary skill, upon reading the reference, would be discouraged from following the path set out in the reference, or would be led in a direction divergent from the path that was taken by the applicant." *Id.*

Here, Gertner acknowledges that a variety of efforts have been made in the prior art to load drugs into wells, grooves or other cavities or reservoirs formed in the surfaces of medical devices. *See, e.g., Gertner* ¶[0022]. However, Gertner teaches that the preformed pores such as those formed in a sintered surface are difficult to load and require high manufacturing temperatures that are incompatible with many bioactive agents. (*See, e.g., Gertner* ¶¶[0023-0025, 0096 and 0105]). According to Gertner, the surface tension of the carrier may preclude the biologically active molecules from thoroughly impregnating the sintered structure. *Id.* at ¶[0023]. Porous surfaces are also subject generally to the disadvantage of poor drug stability. According to Gertner, because a liquid such as blood can enter the pores, the stability of the bioactive material is limited. *Id.* at ¶[0025]. Loading pores, however formed, is also a two-step process, whereas the co-deposition of Gertner achieves a fully loaded matrix in a single step.

The whole point of Gertner is to turn away from and to improve upon preformed porous structures by simultaneously co-depositing the active pharmaceutical agent with metal atoms.

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(See, e.g., *Gertner* ¶¶[0104 and 105]; see also ¶¶[0026, 0033, 0036, 0044-0046, 0061, 0064 and 0102]). This simultaneous or co-deposition is said to overcome the disadvantages of porous surfaces as a drug delivery vehicle on medical devices. See, e.g., *Gertner* ¶[0105].

Thus, Gertner specifically teaches away from the pre-formed porous structures such as those taught by Fleming and Sieradzki. A showing that the prior art teaches away from the combination can rebut a prima facie case of obviousness. *In re Peterson*, 315 F.3d 1325, 1331 (Fed. Cir. 2003). If anything, the smaller porous structures disclosed by Fleming and Sieradzki would further exacerbate the problems associated with the sintering prior art as described by Gertner.

The body of caselaw addressing the motivation to combine for an obviousness rejection under 35 U.S.C. §103(a) is well established. “[S]ection 103 requires assessment of the invention as a whole... showing that an artisan of ordinary skill in the art at the time of invention, confronted by the same problems as the inventor and with no knowledge of the claimed invention, would have selected the various elements from the prior art and combined them in the claimed manner... In other words, section 103 requires some suggestion or motivation, before the invention itself, to make the new combination.” *Princeton Biochemicals, Inc. v. Beckman Coulter, Inc.* 411 F.3d 1332, 1337 (Fed. Cir. 2005) (citing *Ruiz v. A.B. Chance Co.*, 357 F.3d 1270, 1275 (Fed.Cir.2004)). Based upon this caselaw, the Applicants disagree on several grounds with the Examiner’s assertion that the claimed invention would have obvious.

First, the Examiner stated that Fleming or Sieradzki teach a motivation to provide a non-corrosive surface which would reduce unwanted leachings of metallic ions in vivo. Yet, a review of Fleming and Sieradzki failed to identify any teachings that their respective removal processes produce leach resistant coatings, let alone that their removal processes can produce leach resistant coatings on Gertner’s metallic matrix without obliterating Gertner’s matrix itself. Thus, the motivation cited by the Examiner is not present in the cited prior art.

Second, although Gertner teaches the principle of reducing metallic leaching (*Gertner* ¶¶[0166-0168]), it teaches so by adding a protective layer of nickel-phosphorus, not by the removal process as taught by Fleming or Sieradzki. Thus, Gertner teaches the opposite process disclosed in Fleming and Sieradzki, and therefore does not provide a motivation to combine with Fleming or Sieradzki.

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Third, the Examiner did not identify any suggestions or teaching in any of the three references, or in the knowledge of one with ordinary skill in the art, to combine these references that would a) overcome the seeming incompatibility of these references as discussed above in regards to inoperability, or b) teach how the pharmaceutical agent/metallic matrix co-deposition process of Gertner can be used with prior art processes that also produce porous layers.

Thus, for the reasons stated above, Claim 1 would not have been obvious in view of the prior art because the cited references lack any teaching, suggestion or motivation to combine the references, and because one of ordinary skill in the art would not have been motivated to combine the references. For at least the same reasons as Claim 1, Claims 2-9, 11-4, 16-18, 21 and 22 would not have been obvious, and are also patentable for the unique combination of features that Claim 2-9, 11-4, 16-18, 21 and 22 recite.

2. Claims 19 and 20

The Examiner rejected Claims 19 and 20 under 35 U.S.C. §103(a) as obvious over Gertner et al. (U.S. Pat. Pub. No US2005/0106212) in view of Fleming or Sieradzki (U.S. Pat. No. 4,977,038), and further in view of MacGregor (U.S. Pat. No. 4,459,252). According to the Examiner, MacGregor discloses a substrate having a plurality of porous layers.

For at least the same reasons as Claim 1, Claims 19 and 20, which are dependent claims of Claim 1, would not have been obvious and are also patentable for the unique combination of features that Claims 19 and 20 recite.

Furthermore, MacGregor discloses cardiovascular prosthetics with porous surfaces that facilitate tissue overgrowth following prosthesis implantation. MacGregor discloses both flexible polymer porous structures and fixed metallic porous structures created by sintering. As mentioned above, Gertner teaches away from the use of metallic porous surfaces, including sintered metal surfaces, due to difficulty with loading, stability and potentially high manufacturing temperatures. Thus, because Gertner, MacGregor, Fleming and Sieradzki lack any teaching, suggestion or motivation to combine the references, and one of ordinary skill in the art would not be motivated to combine the references, the subject matter of Claim 19 and 20 would not have been obvious.

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Conclusions


Claims 1, 5-9, 14, 16-21 and 42-54 remain pending for consideration. Based on the above amendments and remarks, Applicants submit that each of the pending claims is currently in condition for allowance. Accordingly, Applicants respectfully request a notice of allowance. Applicants have endeavored to respond to each of the issues raised by the Examiner. However, if there remain any unresolved issues that could be resolved via a telephone conference, the Applicants invite the Examiner to initiate the same with Applicants' representative at the telephone number shown below.

Please charge any additional fees, including any fees for additional extension of time, or credit overpayment to Deposit Account No. 11-1410. Please charge any additional fees, including any fees for additional extension of time, or credit overpayment to Deposit Account No. 11-1410.

Respectfully submitted,

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